

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 26 February 2001 (26.02.01)	
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International filing date (day/month/year) 05 June 2000 (05.06.00)	Priority date (day/month/year) 05 June 1999 (05.06.99)
Applicant BRAITHWAITE, Philip	

1. The designated Office is hereby notified of its election made:

☒

in the demand filed with the International Preliminary Examining Authority on:

02 January 2001 (02.01.01)

☐

in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer</p> <p>S. Mafla</p> <p>Telephone No.: (41-22) 338.83.38</p>
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(71) Applicant (*for all designated States except US*): **INNOVATA BIOMED LIMITED** [GB/GB]; The Ziggurat, Grosvenor Road, St. Albans AL1 3HW (GB).

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(72) Inventor; and

(75) Inventor/Applicant (*for US only*): **BRAITHWAITE, Philip** [GB/GB]; ML Laboratories Plc, 13 Alexandra Way, Ashchurch Industrial Estate, Tewkesbury GL20 8NB (GB).

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(74) Agent: **HARRISON GODDARD FOOTE**; Tower House, Merrion Way, Leeds LS2 8PA (GB).

(54) Title: **DELIVERY SYSTEM**

(57) Abstract: There is described a medicament delivery device which comprises a medicament reservoir, a medicament delivery passage and a metering member adapted to transfer a measured dose of medicament from the medicament reservoir to the delivery passage characterised in that the device is provided with a moisture proof barrier. The medicament delivery device is especially suited for use as an inhaler. There is therefore also described an inhaler which provides improved airflow for the dispersion of medicament, and a method of treating patients suffering from a respiratory disorder.

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Delivery System

This invention relates to a novel form of medicament delivery system and to novel methods of treatment.

5

In particular the invention provides a medicament delivery device, such as an inhaler, which is adapted to be moisture resistant and/or provides improved air flow through the device.

- 10 It is well established that delivery devices adapted for the delivery of dry powder medicaments suffer from the problem of contact with moisture. Such problems are particularly when hygroscopic medicaments are used or when climatic conditions give rise to high humidity. Medicament inhalers are known to suffer from such and moisture contamination of dry powder inhalers has long been held to be undesirable
- 15 since the dry powder medicament may become clogged, creating problems in delivering correct dosages of medicament. Furthermore, some inhaled medicaments are themselves inherently moisture sensitive. Therefore, there has long been a desire to provide a dry powder inhaler that is resistant to moisture, that is, one that protects a medicament reservoir from moisture contamination either from the environment or
- 20 from exhalation by a patient using the device and various attempts have been made to mitigate the problem.

- Most attempts which have been made aim to reduce the moisture which comes into contact with a medicament, such attempts generally comprise the use of an additional
- 25 chamber containing a desiccant.

- International Patent Application No WO 98/41261 describes an inhalation device which includes a chamber for containing a desiccant, e.g. silica gel. Whilst the use of a desiccant gel does remove some moisture, the system is disadvantageous in that,
- 30 *inter alia*, the leak paths are too great for the available desiccant to cope with and

therefore the desiccant is only effective for a few hours, whereas there is a need for moisture resistance if at least a few months.

Similarly, International Patent Application No WO 96/08284 describes an inhaler
5 system provided with a reservoir wherein the closed end of the reservoir is also provided with a desiccant cartridge.

International Patent Application No WO 95/32752 also describes a medicament
chamber included in an inhalation apparatus and provided with a container
10 containing a desiccant.

We have now developed a medicament delivery device, e.g. a dry powder inhaler, which is able to provide a moisture proof barrier without the necessity of a desiccant.

15 Therefore, according to the invention we provide a medicament delivery device which comprises a medicament reservoir, a medicament delivery passage and a metering member adapted to transfer a measured dose of medicament from the medicament reservoir to the delivery passage characterised in that the device is provided with a moisture proof barrier.

20 The moisture proof barrier is preferentially a physical barrier as opposed to a chemical barrier, e.g. a desiccant, although it is within the scope of the present invention that a desiccant may be included in addition to the moisture proof barrier if desirable.

25 In a preferred embodiment the moisture proof barrier is positioned so as to prevent the ingress of moisture into the medicament reservoir, so that moisture is prevented from coming into contact with the medicament. In an especially preferred embodiment of the delivery device of the invention, the moisture proof barrier is a
30 moisture proof sealing means.

In a preferred embodiment, the sealing means of the delivery device will operate by the delivery device being adapted to move from an inoperable position, in which the medicament reservoir is sealed, to an operative position, in which the seal is reversibly broken so that measurement and/or delivery of a dose of medicament may take place. The sealing means will generally comprise a resilient sealing member positioned at the end of the reservoir adjacent the metering member. Furthermore, the metering member is preferentially biased towards the resilient sealing member to improve the seal provided. Preferably the resilient sealing member is in a fixed position whilst the metering member moves from an inoperable to an operable position and thus from a sealing to a non-sealing position.

The resilient sealing member preferably comprises a cover adapted to fit the base of the medicament reservoir, the sealing member being provided with an aperture to permit transmission of the medicament. The resilient sealing member may comprise any conventionally known material, for example a natural or synthetic rubber, a silicon or a PTFE material, although other similar materials can be contemplated within the scope of this invention

The moisture proof barrier of the invention may be applied to any conventionally known medicament delivery system. However, in a preferred embodiment, the medicament delivery device is an inhaler. Whilst the moisture proof barrier may be applied to any conventionally known inhaler, it is an especially preferred aspect of the invention for the inhaler to be a dry powder inhaler (DPI). DPI's are known which operate with predetermined doses of medicament, for example, the medicament may be contained in a gelatin capsule which is ruptured to release the medicament. However, a preferred inhaler of the invention is a DPI which comprises a medicament reservoir a metering member which is adapted to measure a selected amount of medicament for inhalation. Thus, in an especially preferred embodiment the metering member is rotatable from an operable to an inoperable position. The metering member may comprise a dispensing member and a moisture resistant member, e.g. a moisture resistant sleeve. In such an embodiment the moisture

resistant member is provided with one or more measuring chambers adapted to measure a predetermined dosage of medicament. Thus, in the operable position, the position of measuring chamber of the metering member corresponds with the aperture in the resilient sealing member so that medicament enters the measuring chamber. The moisture resistant member may then be rotated so that the reservoir is sealed again by the wall of the moisture resistant member. At the same time the medicament is transferred from the measuring chamber of the moisture resistant sleeve to the dispensing chamber of the dispensing member

10 An example of a preferred DPI is CLICKHALER, produced by Innovata Biomed in the UK. Such a device is described in European Patent No 0 539 469. Thus, the metering member may be a frusto conical member such as described in European Patent No 0 539 469.

15 Therefore, the metering member may comprise a frusto conical dispensing member with a corresponding moisture resistant sleeve, such that the sleeve overlies the dispensing member. Thus, the measuring chamber may comprise outer side walls which are provided by an aperture in the wall of the moisture resistant sleeve and the base of the measuring chamber may be provided by the frusto conical wall of the dispensing member. Preferably the moisture resistant sleeve is provided with a plurality of apertures and thereby a plurality of measuring chambers.

The use of the frusto-conical shape in the wall of the metering member containing the measuring chambers allows a good seal to be obtained between the metering member and a seat against which the frusto-conical wall mates.

25 Therefore, the frusto conical metering member may itself comprise a combination of a frusto conical dispensing member and a frusto conical moisture resistant sleeve which forms a snug fit over the dispensing member. The moisture resistant sleeve may itself be moveable eg rotatable, from a sealing to a non-sealing position as herein before described and vice versa. Such a moisture resistant sleeve may

comprise any conventionally known material but is preferentially a plastics material, e.g. the same material as the metering member.

5 The dispensing member and the moisture resistant sleeve can, preferentially, be adapted so as to act together as a medicament measuring/dispensing member. The preferred metering member comprises a dispensing member provided with one or more dispensing cups and a moisture resistant sleeve provided with one or more apertures. Preferably the dispensing member comprises a plurality of dispensing cups and the sleeve comprises a plurality of apertures. It is especially preferred that the
10 dispensing member comprises an equivalent number of dispensing cups to apertures in the sleeve.

We have especially found that if the moisture resistant sleeve comprises a frusto hemispherical cone, then an improved seal is achieved between the medicament
15 reservoir and the sleeve. When a frusto hemispherical cone sleeve is used, the arcuate base of the reservoir is able to make more uniform contact with the curved surface of the cone and therefore an improved seal is achieved. Thus, it is especially preferred that the outer walls of the cone which are hemispherical. Furthermore, the inner walls of the cone are preferably contoured to form a good mate with the frusto
20 conical dispensing member.

Thus, in operation, the metering member may be moved to a first position in which the medicament is transferred to a first measuring chamber in the moisture resistant sleeve, the device is then moved to a second position in which medicament is
25 transferred from the measuring chamber to a dispensing cup in the dispensing member and then to a third position where medicament is delivered to the delivery passage.

The dispensing member may be a conventionally known member such as a frusto
30 conical member described herein and in EP 0 539 469. However, we have also found the use of a moisture resistant sleeve permits a dispensing chamber to be provided

with an air inlet, e.g. an air duct. Previously, the use of an air inlet was felt to be undesirable since it might effect the accuracy of the measurement of the medicament dose. However, by use of a system wherein the medicament is first transferred to a measuring chamber and then subsequently to a dispensing cup, the cup in the
5 dispensing member may be provided with an air inlet without any loss in accuracy of the dosage delivered. Furthermore, improved air flow provides greater likelihood of complete emptying of the dispensing cup and thereby provide an inhaler with improved performance. Clearly, an inhaler with such improved performance is advantageous per se, regardless of whether such an inhaler is moisture resistant.

10

Thus according to an alternative feature of the invention we provide a dry powder inhaler which comprises a medicament reservoir, an inhalation passage for the delivery of the medicament and a metering member adapted to transfer a measured dose of medicament from the medicament reservoir to the inhalation passage
15 characterised in that the metering member comprises a measuring member adapted to measure a pre-defined dosage of medicament and moveable from a measuring to a non-measuring position; and a dispensing member adapted to receive the measured dosage of medicament from the measuring member and to deliver the medicament to the inhalation passage, the dispensing member being moveable from a medicament
20 receiving position to a medicament delivering position.

In the preferred embodiment the dispensing member is provided with one or more medicament dispensing cups, said cups being provided with a duct so as to provide a flow of air through the cup and into the inhalation passage upon operation of the
25 device.

By the term dry powder we mean a medicament in finely divided form.

A variety of medicaments may be administered by using the inhaler of the invention,
30 optionally with a conventionally known pharmaceutically acceptable adjuvant, diluent or carrier. Such medicaments are generally antibiotics, bronchodilators or

- other anti-asthma drugs. Such medicaments include, but are not limited to β_2 -agonists, e.g. fenoterol, formoterol, pirbuterol, reproterol, rimiterol, salbutamol, salmeterol and terbutaline; non-selective beta-stimulants such as isoprenaline; xanthine bronchodilators, e.g. theophylline, aminophylline and choline theophyllinate; anticholinergics, e.g. ipratropium bromide; mast cell stabilisers, e.g. sodium cromoglycate and ketotifen; bronchial anti-inflammatory agents, e.g. nedocromil sodium; and steroids, e.g. beclomethasone dipropionate, fluticasone, budesonide and flunisolide; and combinations thereof.
- 10 Specific combinations of medicaments which may be mentioned include combinations of steroids, such as, beclomethasone dipropionate, fluticasone, budesonide and flunisolide; and combinations of to β_2 -agonists, such as, formoterol and salmeterol. It is also within the scope of this invention to include combinations of one or more of the aforementioned steroids with one or more of the
- 15 aforementioned β_2 -agonists.

The inhaler of the invention is especially suitable for use in the treatment or alleviation of respiratory disorders. Thus according to the invention we also provide a method of administering a dry powder inhalation medicament using an inhaler as

20 hereinbefore described.

We further provide a method of treatment of a patient with a respiratory disorder which comprises the administration of a combination of medicaments using an inhaler as hereinbefore described.

- 25 The invention will now be described by way of example only and with reference to the accompanying drawings in which:

Figure 1 is a perspective view of an inhalation device of the invention;

Figure 2 is a schematic representation of the sealing and measuring mechanism.

Figure 3 is a perspective view of a moisture resistant sleeve comprising a frusto hemispherical cone, and

Figure 4 is a cross-sectional view of a moisture resistant sleeve comprising a frusto hemispherical cone.

5

With reference to Fig 1, a dry powder inhaler (1) comprises a medicament reservoir (2) comprising an essentially conical member; an inhalation passage (3) and a metering member (4). The inhalation passage (3) is connected to the medicament reservoir (2) by a reservoir support (5) and is itself connected to recess (6) which provides a seat for the metering member (4). The metering member (4) is rotatable about an axis (7) from a medicament receiving position, to a medicament delivery position and then to an emptying position to allowing any residual medicament to be emptied into a waste box (8).

15 The recess (6) is essentially frusto conical in shape to enable it to provide a seal for the metering member (4). The metering member (4) comprises a frusto conical moisture resistant sleeve (9) which forms a snug fit between recess (6) and a dispensing member (10). The dispensing member (10) is also provided with a back plate (11).

20

The moisture resistant sleeve (9) abuts against the resilient seal (9a) to form a moisture resistant seal.

25

The moisture resistant sleeve (9) is also provided with a plurality of measuring chambers which comprise apertures (12) dimensioned to measure a predetermined amount of medicament and to fit over cups (13) in the dispensing member (10). In a preferred embodiment, each of the cups (13) are also provided with a duct (14). The medicament reservoir (2) is also provided with a moisture resistant, eg foil, cover (15) at it's end (16) distal from the metering member (4).

30

With reference to Figure 2, in which Figure 2a the metering device is in a closed position,

Figure 2b the metering device is in a measuring position,

Figure 2c the metering device is in a seal transitory position,

5 Figure 2d the metering device is in a medicament transfer position,

Figure 2e the metering device is in a medicament delivery position; and

Figure 2f the metering device is returned to the closed position.

10 In Figure 2a the metering device 4 is in the closed position and the medicament reservoir (2) is isolated and a seal formed between the sealing member (17) and the surface (18) of the moisture resistant sleeve (9). In Figure 2b, the moisture resistant sleeve (9) is rotated in an anti clockwise direction so that the aperture (12) corresponds with the aperture/measuring chamber (19) in the sealing member (17). The aperture/measuring chamber (19) forms a cup with the surface (20) of the
15 dispensing member (10).

In Figure 2c the moisture resistant sleeve (9) is further rotated so that the aperture/measuring chamber (19) sits below the sealing member (17). The internal edge (21) of the sealing member (17) scrapes any excess medicament from the
20 aperture/measuring chamber (19) to leave a measured dose.

In Figure 2d the dispensing member (10) is rotated in an anticlockwise direction so that the dispensing cup (13) corresponds with the aperture (12) allowing medicament to transfer from the aperture (12) to the dispensing cup (13).

25

In Figure 2e both the dispensing member (10) and the moisture resistant sleeve (9) are rotated anticlockwise to expose them and the medicament to the inhalation passage (3). The patient can then inhale the medicament.

30 In Figure 2f the inhalation device remains in the closed position ready for use.

With reference to Figures 3 and 4, a moisture resistant sleeve (9) comprises a frusto hemispherical cone (22) wherein the outer surface (23) is arcuate. The inner surface (24) acts as a female member to form a snug fit with the frusto conical dispensing member (10). Downward pressure in the medicament reservoir (2) ensures a constant moisture tight seal between the sealing member (17) and the frusto hemispherical cone (22). Furthermore, referring to Figure 4c, the leading edge (25) of the sealing member (17) is capable of acting as a scraper or a cleaning edge, removing any excess medicament from the measuring chamber upon rotation of the metering member.

A variety of mechanisms may be used for the operation of the inhaler. One preferred mechanism is for movement from the closed to the measuring position to be achieved by removal of a mouth piece which is operably linked to the moisture resistor. Movement from the measuring position to the transitory position would use a mechanism similar to that described in EP 0 539 469, e.g. by depressing the button half way. Movement to the transfer position being achieved by further depressing the button, and then depression completely, moving the metering cone and the moisture resistor to the delivery position.

CLAIMS

1. A medicament delivery device which comprises a medicament reservoir, a medicament delivery passage and a metering member adapted to transfer a measured dose of medicament from the medicament reservoir to the delivery passage characterised in that the device is provided with a moisture proof barrier.
5
2. A medicament delivery device according to Claim 1 characterised in that the moisture proof barrier is a moisture proof sealing means.
10
3. A medicament delivery device according to claim 1 characterised in that the moisture proof barrier is positioned to prevent ingress of moisture into the medicament reservoir.
15
4. A medicament delivery device according to Claim 1 wherein the sealing means is adapted to move from an inoperable position in which the medicament reservoir is sealed, to an operable position in which the seal is broken so that measurement and/or delivery of a dose of medicament may take place.
20
5. A medicament delivery device according to Claim 1 wherein the sealing means comprises a resilient sealing member positioned at the end of the medicament reservoir adjacent the metering member.
25
6. A medicament delivery device according to Claim 5 wherein the metering member is biased towards the sealing member.
7. A medicament delivery device according to claim 1 characterised in that the delivery device is an inhaler.
30

8. A medicament delivery device according to claim 7 characterised in that the inhaler is a dry powder inhaler.
- 5 9. A medicament delivery device according to Claim 4 characterised in that the metering member is rotatable from an operable to an inoperable position.
- 10 10. A medicament delivery device according to Claim 1 characterised in that the metering member comprises a combination of a dispensing member and an outer sleeve.
11. A medicament delivery device according to Claim 10 characterised in that the outer sleeve is a moisture resistant sleeve
- 15 12. A medicament delivery device according to Claim 12 characterised in that the wherein the moisture resistant sleeve is adapted to act as a medicament measuring device.
- 20 13. A medicament delivery device according to claim 12 wherein the moisture resistant sleeve is a frusto hemispherical cone.
- 25 14. A medicament delivery device according to Claim 1 characterised in that the device may be moved to a first position in which the medicament is transferred to a measuring chamber, the device is then moved to a second position in which medicament is transferred to a dispensing chamber and to a third position where medicament is delivered into the delivery passage.
- 30 15. A medicament delivery device which is an inhaler and comprises a medicament reservoir, an inhalation passage and a metering member provided with at least one dispensing cup and adapted to transfer a measured dose of medicament from the medicament reservoir to the inhalation passage characterised in that the dispensing cup is provided with an air duct.

16. An inhaler according to Claim 15 characterised in that the device is provided with a moisture proof barrier.
- 5 17. An inhaler comprising a medicament reservoir, an inhalation passage for the delivery of the medicament and a metering member adapted to transfer a measured dose of medicament from the medicament reservoir to the inhalation passage characterised in that the metering member comprises a measuring member adapted to measure a pre-defined dosage of medicament
10 and moveable from a measuring to a non-measuring position; and a dispensing member adapted to receive the measured dosage of medicament from the measuring member and to deliver the medicament to the inhalation passage, the dispensing member being moveable from a medicament receiving position to a medicament delivering position.
- 15 18. An inhaler according to Claim 17 wherein the second member is provided with one or more medicament receiving cups, said cups being provided with an air duct so as to provide a flow of air through the passage and the cup into the inhalation passage upon operation of the device.
- 20 19. An inhaler comprising a medicament reservoir, an inhalation passage for the delivery of the medicament and a metering member adapted to transfer a measured dose of medicament from the medicament reservoir characterised in that the metering member is provided with a duct to allow air to be sucked
25 through the metering member upon inhalation by a patient.
20. An inhaler according to claim 19 characterised in that the metering member comprises an outer sleeve and a dispensing member.
- 30 21. A medicament delivery device according to claim 20 characterised in that the duct is part of a measuring cup in the dispensing member.

22. A method of administering a medicament by inhalation which comprises the use by a patient of an inhaler according to claim 1.
- 5 23. A method of administering a dry powder inhalation medicament using an inhaler according to Claim 7.
24. A method of treatment of a patient with a respiratory disorder which comprises the administration of a combination of medicaments using an inhaler according to Claim 7.
- 10 25. A medicament delivery device substantially as described with reference to the accompanying drawings.

15

20

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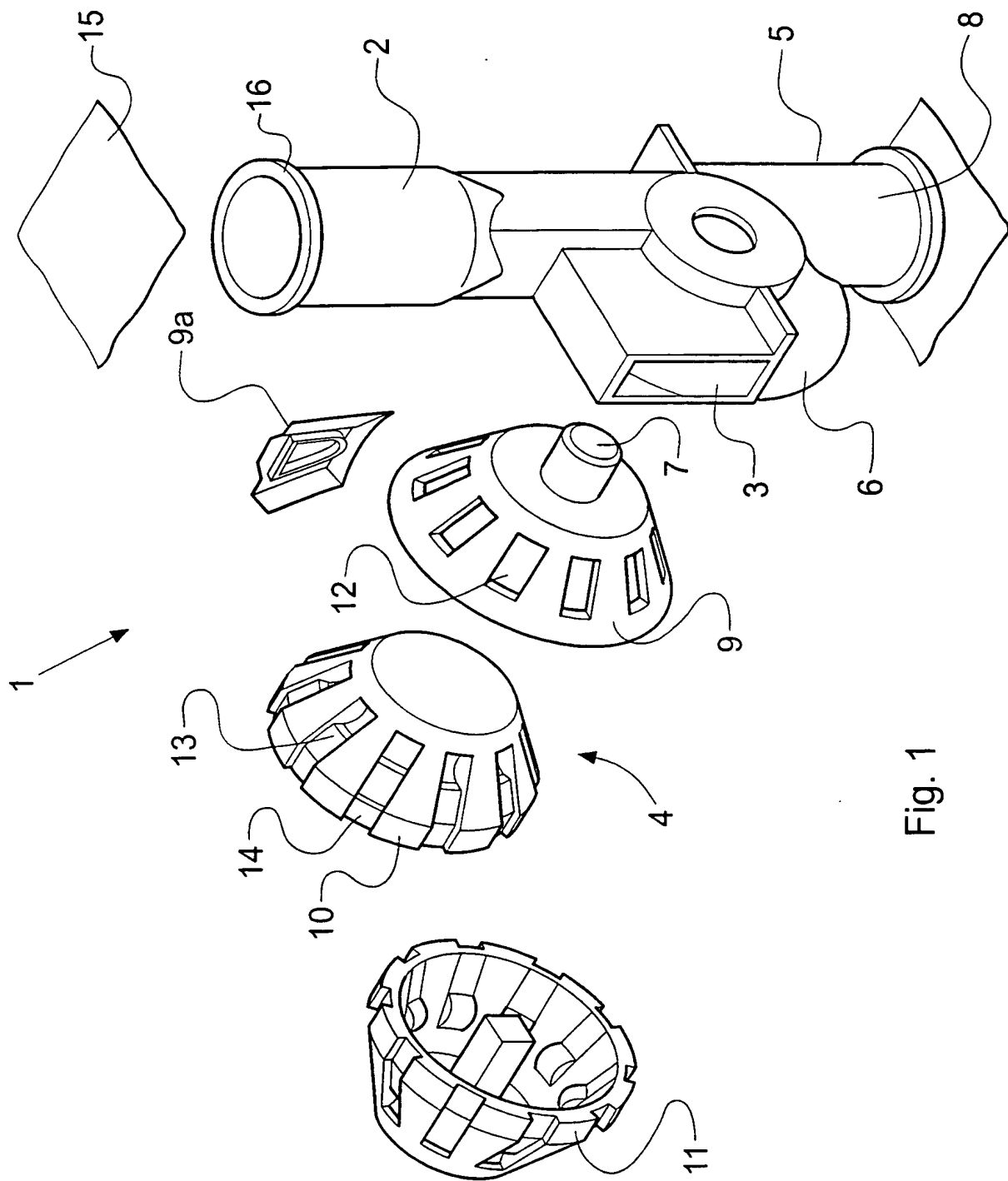


Fig. 1

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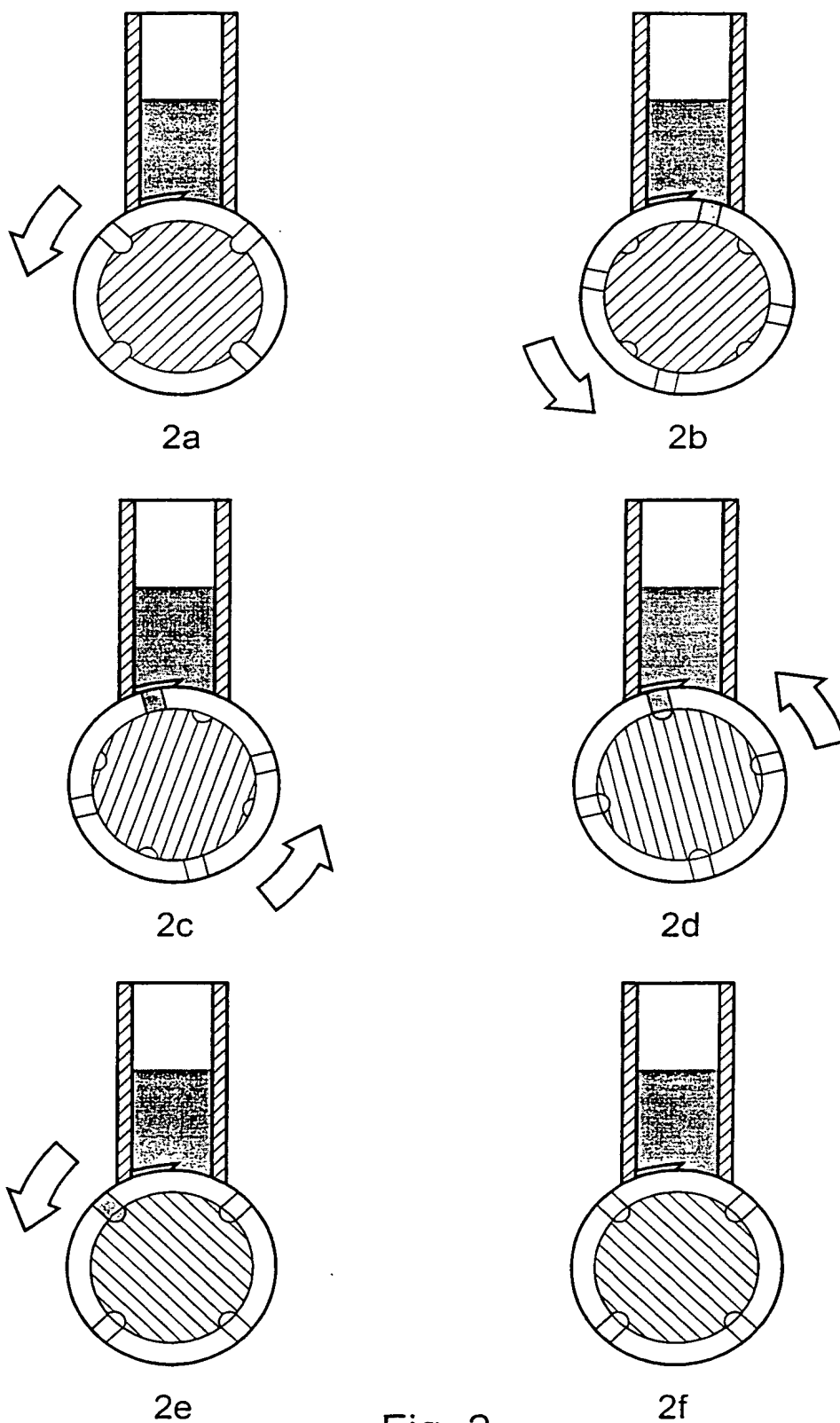


Fig. 2

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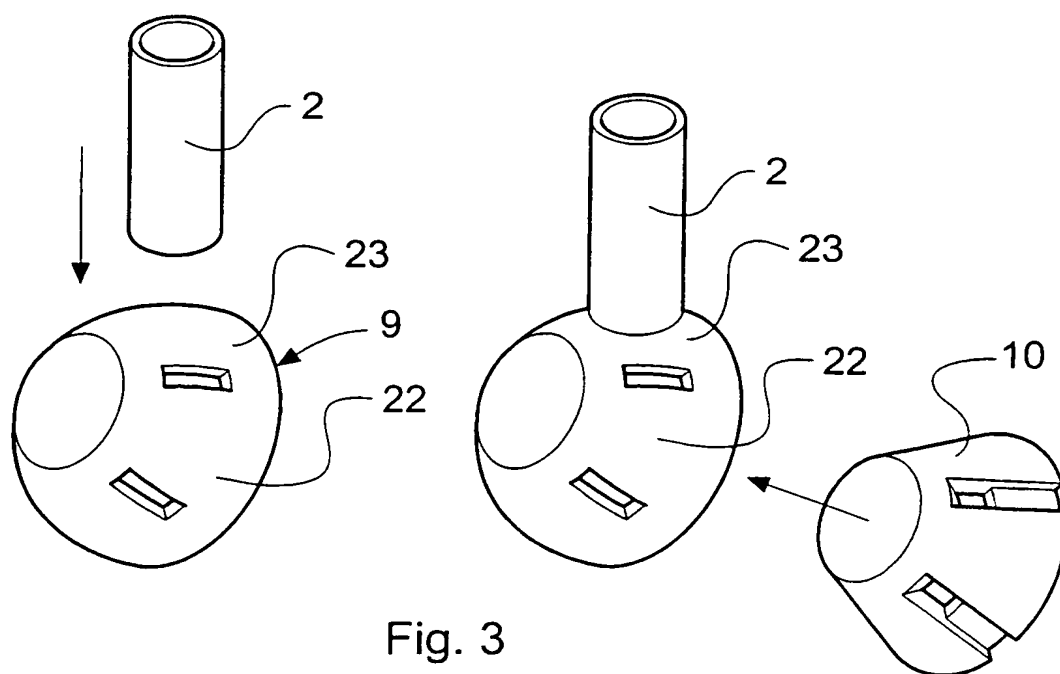


Fig. 3

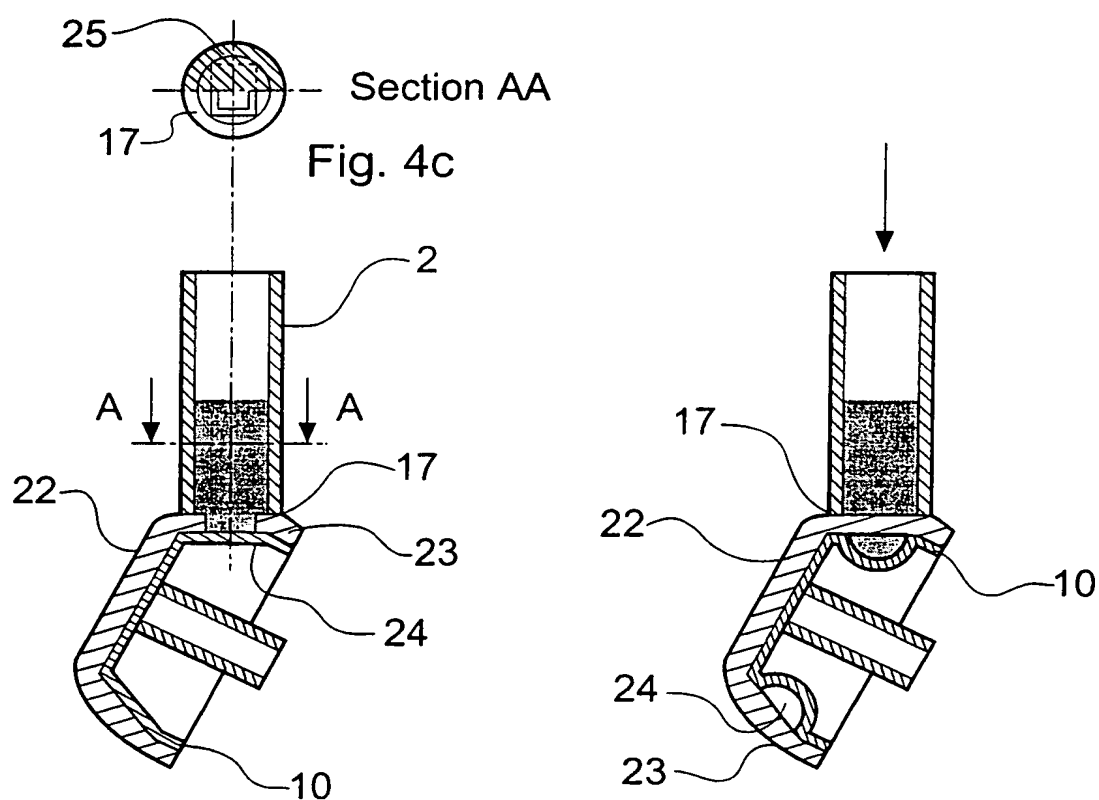


Fig. 4a

Fig. 4b

Fig. 4

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REC'D 16 OCT 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference SPG/P36086WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/02017	International filing date (day/month/year) 05/06/2000	Priority date (day/month/year) 05/06/1999
International Patent Classification (IPC) or national classification and IPC A61M15/00		
Applicant INNOVATA BIOMED LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
 - ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 02/01/2001	Date of completion of this report 12.10.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Hagberg, A Telephone No. +49 89 2399 7432 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02017

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

3-10 as originally filed

1,2,2a as received on 05/07/2001 with letter of 02/07/2001

Claims, No.:

1-25 as received on 05/07/2001 with letter of 02/07/2001

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02017

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 15-25.

because:

☒ the said international application, or the said claims Nos. 22-25 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 15-25.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02017

- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-14.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The subject-matter of claims 22-24 are methods for treatment of the human body by therapy, therefore no opinion has been established with regard to these claims (Rule 39.1(iv) PCT).
2. No opinion has been established with regard to claim 25 because the subject-matter of this claim does not meet the requirements of the PCT, Rule 6.2(a).

Re Item IV

Lack of unity of invention

The International Preliminary Examining Authority agrees with the objection of lack of unity of invention raised by the International Searching Authority for the following reasons:

D1 discloses an inhaler with reservoir, delivery passage, metering member and a moisture proof barrier.

Independent claim 1 therefore defines no special technical feature within the meaning of PCT Rule 13.2.

The following features are special technical feature within the meaning of PCT Rule 13.2:

In independent claims 15 and 19; a metering member with air duct.

In independent claim 17; a metering member with movable measuring and dispensing parts.

These special technical feature are different and solve different technical problems. The application therefore appears to relate to three different inventions, namely

1. Claims 1-14: Medicament delivery device comprising reservoir, delivery passage, metering member and a moisture proof barrier.
2. Claims 15-16, 19-21: Inhaler comprising reservoir, inhalation passage and metering member with air duct.

3. Claims 17-18: Inhaler comprising reservoir, inhalation passage and metering member with movable measuring and dispensing parts.

These three inventions are not so linked as to form a single general inventive concept because they do not have any special technical feature in common.

Hence, the requirement of unity is not met (Rule 13.1 PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document:

D1: EP-A-0 520 440 (Schering) 30 December 1992

2. D1 discloses (column 9, line 40 - column 10, line 40, column 14, lines 37-45, figures): A medicament delivery device (110) which comprises a medicament reservoir (136), a medicament delivery passage (132), a metering member (146) adapted to transfer a measured dose of medicament from the medicament reservoir to the delivery passage, and a moisture proof barrier (116, 192).

The subject-matter of claim 1 therefore differs from this known medicament delivery device in that the moisture proof barrier comprises a resilient sealing member in a fixed position.

This feature is novel and cannot be derived in an obvious manner from the prior art.

The subject-matter of claim 1 is therefore novel and inventive (Article 33(2)(3) PCT).

3. Claims 2-14 are dependent on claim 1 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

Re Item VII

Certain defects in the international application

1. In figure 2, it appears that the reference signs referred to on page 9 are missing.
2. It appears that a word is missing in the text ' Such problems are particularly when...' on page 1, lines 11-12.

Delivery System

This invention relates to a novel form of medicament delivery system and to novel methods of treatment.

5

In particular the invention provides a medicament delivery device, such as an inhaler, which is adapted to be moisture resistant and/or provides improved air flow through the device.

10 It is well established that delivery devices adapted for the delivery of dry powder medicaments suffer from the problem of contact with moisture. Such problems are particularly when hygroscopic medicaments are used or when climatic conditions give rise to high humidity. Medicament inhalers are known to suffer from such and moisture contamination of dry powder inhalers has long been held to be undesirable
15 since the dry powder medicament may become clogged, creating problems in delivering correct dosages of medicament. Furthermore, some inhaled medicaments are themselves inherently moisture sensitive. Therefore, there has long been a desire to provide a dry powder inhaler that is resistant to moisture, that is, one that protects a medicament reservoir from moisture contamination either from the environment or
20 from exhalation by a patient using the device and various attempts have been made to mitigate the problem.

Most attempts which have been made aim to reduce the moisture which comes into contact with a medicament, such attempts generally comprise the use of an additional
25 chamber containing a desiccant.

International Patent Application No WO 98/41261 describes an inhalation device which includes a chamber for containing a desiccant, e.g. silica gel. Whilst the use of a desiccant gel does remove some moisture, the system is disadvantageous in that,
30 *inter alia*, the leak paths are too great for the available desiccant to cope with and

therefore the desiccant is only effective for a few hours, whereas there is a need for moisture resistance if at least a few months.

5 Similarly, International Patent Application No WO 96/08284 describes an inhaler system provided with a reservoir wherein the closed end of the reservoir is also provided with a desiccant cartridge.

10 International Patent Application No WO 95/32752 also describes a medicament chamber included in an inhalation apparatus and provided with a container containing a desiccant.

15 European Patent Application No. EP 0520 440, Ambrosio et al, describes a dry powder inhaler which includes a moisture resistant barrier in the form of a flap which is designed to prevent exhaled air from a patient contaminating the medicament held in the reservoir.

20 US Patent No. 3,854,626, Krechmar et al, describes a pill dispensing system which comprises a moveable mechanism which prevents the ingress of moisture whilst permitting the dispensing of one or more pills.

We have now developed a medicament delivery device, e.g. a dry powder inhaler, which is able to provide a moisture proof barrier without the necessity of a desiccant.

25 Therefore, according to the invention we provide a medicament delivery device which comprises a medicament reservoir, a medicament delivery passage and a metering member adapted to transfer a measured dose of medicament from the medicament reservoir to the delivery passage characterised in that the device is provided with a moisture proof barrier.

30 The moisture proof barrier is preferentially a physical barrier as opposed to a chemical barrier, e.g. a desiccant, although it is within the scope of the present

invention that a desiccant may be included in addition to the moisture proof barrier if desirable.

5 In a preferred embodiment the moisture proof barrier is positioned so as to prevent the ingress of moisture into the medicament reservoir, so that moisture is prevented from coming into contact with the medicament. In an especially preferred embodiment of the delivery device of the invention, the moisture proof barrier is a moisture proof sealing means.

**REVISED CLAIMS FOR INTERNATIONAL PATENT APPLICATION
NO. PCT/GB00/02017**

- 5 1. A medicament delivery device (1) which comprises a medicament reservoir (2), a medicament delivery passage (3) and a metering member (4) adapted to transfer a measured dose of medicament from the medicament reservoir (2) to the delivery passage (3), the device (1) being provided with a moisture proof barrier (9) characterised in that the moisture proof barrier (9) comprises a resilient sealing member in a fixed position.
- 10 2. A medicament delivery device (1) according to Claim 1 characterised in that the moisture proof barrier is a moisture proof (9) sealing means.
- 15 3. A medicament delivery device (1) according to claim 1 characterised in that the moisture proof barrier (9) is positioned to prevent ingress of moisture into the medicament reservoir (2).
- 20 4. A medicament delivery device (1) according to Claim 1 wherein the sealing means is adapted to move from an inoperable position in which the medicament reservoir (2) is sealed, to an operable position in which the seal is broken so that measurement and/or delivery of a dose of medicament may take place.
- 25 5. A medicament delivery device (1) according to Claim 1 wherein the sealing means comprises a resilient sealing member positioned at the end of the medicament reservoir (2) adjacent the metering member (4).
- 30 6. A medicament delivery device according to Claim 5 wherein the metering member (4) is biased towards the sealing member (9).
7. A medicament delivery device (1) according to claim 1 characterised in that the delivery device is an inhaler.

8. A medicament delivery device (1) according to claim 7 characterised in that the inhaler is a dry powder inhaler.
- 5 9. A medicament delivery device (1) according to Claim 4 characterised in that the metering member (4) is rotatable from an operable to an inoperable position.
- 10 10. A medicament delivery device (1) according to Claim 1 characterised in that the metering member (4) comprises a combination of a dispensing member (10) and an outer sleeve.
11. A medicament delivery device (1) according to Claim 10 characterised in that the outer sleeve is a moisture resistant sleeve (9).
- 15 12. A medicament delivery device (1) according to Claim 11 characterised in that the moisture resistant sleeve (9) is adapted to act as a medicament measuring device.
- 20 13. A medicament delivery device (1) according to claim 12 wherein the moisture resistant sleeve is a frusto hemispherical cone (22).
- 25 14. A medicament delivery device (1) according to Claim 1 characterised in that the device may be moved to a first position in which the medicament is transferred to a measuring chamber; the device is then moved to a second position in which medicament is transferred to a dispensing chamber and to a third position where medicament is delivered into the delivery passage (3).
- 30 15. A medicament delivery device (1) which is an inhaler and comprises a medicament reservoir (2), an inhalation passage (3) and a metering member (4) provided with at least one dispensing cup (13) and adapted to transfer a measured dose of medicament from the medicament reservoir (2) to the

inhalation passage (3) characterised in that the dispensing cup (13) is provided with an air duct (14).

- 5 16. An inhaler according to Claim 15 characterised in that the device is provided with a moisture proof barrier.
- 10 17. An inhaler comprising a medicament reservoir (2), an inhalation passage (3) for the delivery of the medicament and a metering member (4) adapted to transfer a measured dose of medicament from the medicament reservoir (2) to the inhalation passage (3) characterised in that the metering member (4) comprises a measuring member adapted to measure a pre-defined dosage of medicament and moveable from a measuring to a non-measuring position; and a dispensing member adapted to receive the measured dosage of medicament from the measuring member and to deliver the medicament to the inhalation passage, the dispensing member being moveable from a medicament receiving position to a medicament delivering position.
- 15 18. An inhaler according to Claim 17 wherein the second member is provided with one or more medicament receiving cups, said cups being provided with an air duct so as to provide a flow of air through the passage and the cup into the inhalation passage upon operation of the device.
- 20 19. An inhaler comprising a medicament reservoir (2), an inhalation passage (3) for the delivery of the medicament and a metering member (4) adapted to transfer a measured dose of medicament from the medicament reservoir (2) characterised in that the metering member (4) is provided with a duct (14) to allow air to be sucked through the metering member upon inhalation by a patient.
- 25 20. An inhaler according to claim 19 characterised in that the metering member (4) comprises an outer sleeve and a dispensing member (10).
- 30

21. A medicament delivery device (1) according to claim 20 characterised in that the duct is part of a measuring cup in the dispensing member.
22. A method of administering a medicament by inhalation which comprises the use by a patient of an inhaler according to claim 1.
23. A method of administering a dry powder inhalation medicament using an inhaler according to Claim 7.
24. A method of treatment of a patient with a respiratory disorder which comprises the administration of a combination of medicaments using an inhaler according to Claim 7.
25. A medicament delivery device (1) substantially as described with reference to the accompanying drawings.

15

20 P36086WO Revised Claims

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

HARRISON GODDARD FOOTE
Tower House
Merrion Way
Leeds LS2 8PA
GRANDE BRETAGNE

16.OCT.2001* 1782

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year) 12.10.2001

Applicant's or agent's file reference
SPG/P36086WO

IMPORTANT NOTIFICATION

International application No.
PCT/GB00/02017

International filing date (day/month/year)
05/06/2000

Priority date (day/month/year)
05/06/1999

Applicant
INNOVATA BIOMED LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Novoa, C

Tel. +49 89 2399-2718



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/02017

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*):

Description, pages:

3-10 as originally filed

1,2,2a as received on 05/07/2001 with letter of 02/07/2001

Claims, No.:

1-25 as received on 05/07/2001 with letter of 02/07/2001

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SPG/P36086W0	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 02017	International filing date (day/month/year) 05/06/2000	(Earliest) Priority Date (day/month/year) 05/06/1999
Applicant INNOVATA BIOMED LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

ational application No.
PCT/GB 00/02017

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 22-24
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☒ Claims Nos.: 25
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
Claim 25 is written in a form which is contrary to PCT Rule 6.2(a).
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-14

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 00/ 02017

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Line 1: insert "(1)" after "device"
Line 2: insert "(2)" after "reservoir", insert "(3)" after "passage" and
insert "(4)" after "member"
Line 4: insert "(9)" after "barrier"

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 25

Claim 25 is written in a form which is contrary to PCT Rule 6.2(a).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-14

Medicament delivery device comprising reservoir, delivery passage, metering member and moisture proof barrier.

2. Claims: 15-16, 19-21

Inhaler with reservoir, inhalation passage, and metering member with dispensing cup provided with an air duct.

3. Claims: 17-18

Inhaler with reservoir, inhalation passage, and metering member with movable measuring and dispensing parts.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02017

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61M15/00 A61J1/00 B65D83/00 B65D81/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61M A61J B65D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 503 144 A (BACON RAYMOND) 2 April 1996 (1996-04-02) the whole document ---	1-5,7-9, 14
X	FR 2 753 791 A (TEBRO) 27 March 1998 (1998-03-27) the whole document ---	1-5,7-9
X	DE 195 30 240 A (BRENDDEL GERHARD) 20 February 1997 (1997-02-20) the whole document ---	1-4,7-9
X	EP 0 520 440 A (SCHERING CORP) 30 December 1992 (1992-12-30) column 9, line 32 -column 15, line 14; figures 5-21 --- -/--	1-4,7-9



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

28 August 2000

Date of mailing of the international search report

- 7. DEZ. 2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Jameson, P

INTERNATIONAL SEARCH REPORT

International Application No

P GB 00/02017

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 854 626 A (KRECHMAR J) 17 December 1974 (1974-12-17) the whole document ---	1-4
A	EP 0 539 469 A (BRAITHWAITE PHILIP WILSON) 5 May 1993 (1993-05-05) cited in the application the whole document ---	1-14
A	US 4 174 034 A (HOO WILLIAM K C) 13 November 1979 (1979-11-13) abstract; figure 3 ---	1
A	GB 1 573 551 A (STOCKHAUSEN & CIE CHEM FAB) 28 August 1980 (1980-08-28) the whole document -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

GB 00/02017

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5503144	A	02-04-1996	AT 144155 T AU 647851 B AU 8932691 A CA 2091366 A,C CN 1062297 A,B CY 1999 A DE 69122769 D DE 69122769 T DK 561838 T EP 0561838 A ES 2092581 T FI 931980 A WO 9210229 A GR 3021495 T HK 48397 A IE 76470 B IL 100341 A JP 2535296 B JP 6503009 T NO 305785 B NZ 240833 A PT 99805 A,B ZA 9109521 A	15-11-1996 31-03-1994 08-07-1992 16-06-1992 01-07-1992 05-12-1997 21-11-1996 03-04-1997 18-11-1996 29-09-1993 01-12-1996 30-04-1993 25-06-1992 31-01-1997 25-04-1997 22-10-1997 27-11-1995 18-09-1996 07-04-1994 26-07-1999 27-09-1993 31-01-1994 26-08-1992
FR 2753791	A	27-03-1998	WO 9811929 A EP 0934089 A	26-03-1998 11-08-1999
DE 19530240	A	20-02-1997	NONE	
EP 0520440	A	30-12-1992	AT 137675 T AU 661857 B AU 2253692 A CA 2112576 A,C CN 1067822 A,B CZ 9302883 A DE 69210607 D DE 69210607 T DK 592601 T EP 0592601 A ES 2086759 T FI 935792 A GR 3020326 T HK 220596 A HU 67275 A,B IE 74886 B IL 102316 A JP 2780871 B JP 6503026 T KR 9706097 B MX 9203524 A NO 934811 A NZ 243314 A SG 43834 A SK 147593 A WO 9300123 A ZA 9204718 A	15-05-1996 10-08-1995 25-01-1993 07-01-1993 13-01-1993 13-04-1994 13-06-1996 26-09-1996 10-06-1996 20-04-1994 01-07-1996 22-12-1993 30-09-1996 03-01-1997 28-03-1995 13-08-1997 14-11-1996 30-07-1998 07-04-1994 23-04-1997 01-12-1993 14-02-1994 26-07-1994 14-11-1997 10-08-1994 07-01-1993 24-02-1993
US 3854626	A	17-12-1974	NONE	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

GB 00/02017

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0539469	A	05-05-1993	AU 657914 B BR 9106693 A DE 69108912 D DE 69108912 T FI 930105 A FI 991213 A GR 3015854 T JP 2891541 B JP 8505290 T KR 184288 B NO 304218 B NO 982791 A AT 120970 T AT 114981 T AU 8191691 A CA 2086415 A,C DE 69105756 D DE 69105756 T DK 539469 T DK 573128 T EP 0573128 A ES 2072006 T ES 2068041 T WO 9200771 A GB 2260498 A,B GB 2265552 A,B GR 3015317 T NZ 238958 A NZ 248398 A US 5437270 A US 5657748 A ZA 9105437 A	30-03-1995 29-06-1993 18-05-1995 31-08-1995 12-01-1993 28-05-1999 31-07-1995 17-05-1999 11-06-1996 01-04-1999 16-11-1998 17-06-1998 15-04-1995 15-12-1994 04-02-1992 14-01-1992 19-01-1995 18-05-1995 03-07-1995 06-03-1995 08-12-1993 01-07-1995 01-04-1995 23-01-1992 21-04-1993 06-10-1993 30-06-1995 26-07-1995 26-07-1995 01-08-1995 19-08-1997 25-03-1992
US 4174034	A	13-11-1979	NONE	
GB 1573551	A	28-08-1980	DE 2623626 A AT 364117 B AT 373377 A BE 855027 A CH 614906 A DK 229577 A FR 2352729 A LU 77408 A NL 7705739 A,B, SE 412513 B SE 7706134 A	01-12-1977 25-09-1981 15-02-1981 25-11-1977 28-12-1979 27-11-1977 23-12-1977 09-09-1977 29-11-1977 10-03-1980 27-11-1977